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July 18, 2005

Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, rm. 1061
Rockville, MD 20852.

Dear Professional Staff:

Amphastar Pharmaceuticals, Inc. (Amphastar) hereby submits additional comments on Aventis' Citizen Petition 2003P-0064, in quadruplicate. In response to Aventis' March 17, 2005 comment to this above referenced petition, Amphastar performed additional comparative analysis of Lovenox® and Amphastar's proposed Enoxaparin Sodium Injection product. Analysis was performed by a cetyltrimethylammonium coated strong anion exchange method (CAT-SAX/UV) and a strong anion exchange methodology (SAX LC/UV) following heparinase depolymerization. The results of these tests clearly demonstrate the chemical equivalence of Active Pharmaceutical Ingredient contained in Lovenox and in Amphastar's enoxaparin sodium injection, in direct contradiction to Aventis March 17 comments.

Amphastar continues to urge the Commissioner to deny Citizen Petition 2003P-0064 based upon the cumulative comments submitted by Amphastar in opposition to the petition.

Very truly yours,

Stephen A. Campbell, Esq.
Senior Vice President, Regulatory Affairs

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Docket Number 2003P-0064: Amphastar's Response To Aventis' March 17, 2005 Comment (RC2)

Aventis filed the above referenced Citizen Petition on February 19, 2003. In an attempt to thwart generic competition, Aventis argued, among other things, that the Food and Drug Administration (FDA) should refrain from approving any abbreviated new drug application (ANDA) citing Lovenox (enoxaparin), until such time as the product has been "fully characterized." The premise of Aventis' arguments is that, due to the complexity of the product, a generic applicant will not be able to demonstrate "sameness" unless it uses Aventis' manufacturing process or conducts clinical testing. Aventis' arguments are flawed because they ignore the applicable regulatory scheme. There is no requirement that states that in order to demonstrate sameness the manufacturing process for the innovator and the generic must be the same. In addition, by suggesting that the FDA require clinical testing of a generic product, Aventis is asking the FDA to require more than maybe legally required in an ANDA. See 21 U.S.C. § 355(j)(2)(A).

On June 4, 2004, the FDA submitted to this docket a May 13, 2004 letter from Amphastar in response to Aventis' Citizen's Petition. Amphastar's May 13 letter described data and information, including chromatographic studies, that taken together demonstrate that Amphastar's enoxaparin product is the same as Aventis' Lovenox.

On October 13, 2004, Aventis submitted comments on Amphastar's response. Aventis criticized the data and test results submitted by Amphastar in its May 13, 2004 letter

On November 23, 2004, Amphastar responded to Aventis' criticisms by pointing out that in its October 13, 2004 comments, Aventis used the chromatogram of entire distribution by an analytic method to compare Amphastar's chromatography obtained by preparation of some major oligosaccharides. Aventis also compared the chromatogram to a different SAX method. By doing this, Aventis was comparing apples to oranges.

On March 17, 2005, Aventis submitted additional comments, which continue to argue that Amphastar's comparisons of its product to Lovenox are somehow "flawed."

In order to provide clarity, Amphastar has conducted a further comparison study for Lovenox manufactured by Aventis and Amphastar's Enoxaparin. The results are provided herein as Figures 1 and 2.

(1) By LC/UV method, chromatograms of the entire distribution of oligosaccharides in Enoxaparin is provided in Fig. 1. (Amphastar's Enoxaparin in blue and Aventis' Lovenox in red.)

(2) By LC/UV method, chromatograms of Heparinase-hydrolyzed Enoxaparin is provided in Fig. 2. (Amphastar's Enoxaparin in blue and Aventis' Lovenox in red.)

Both of these studies demonstrate that the two products have the same chromatogram profiles.

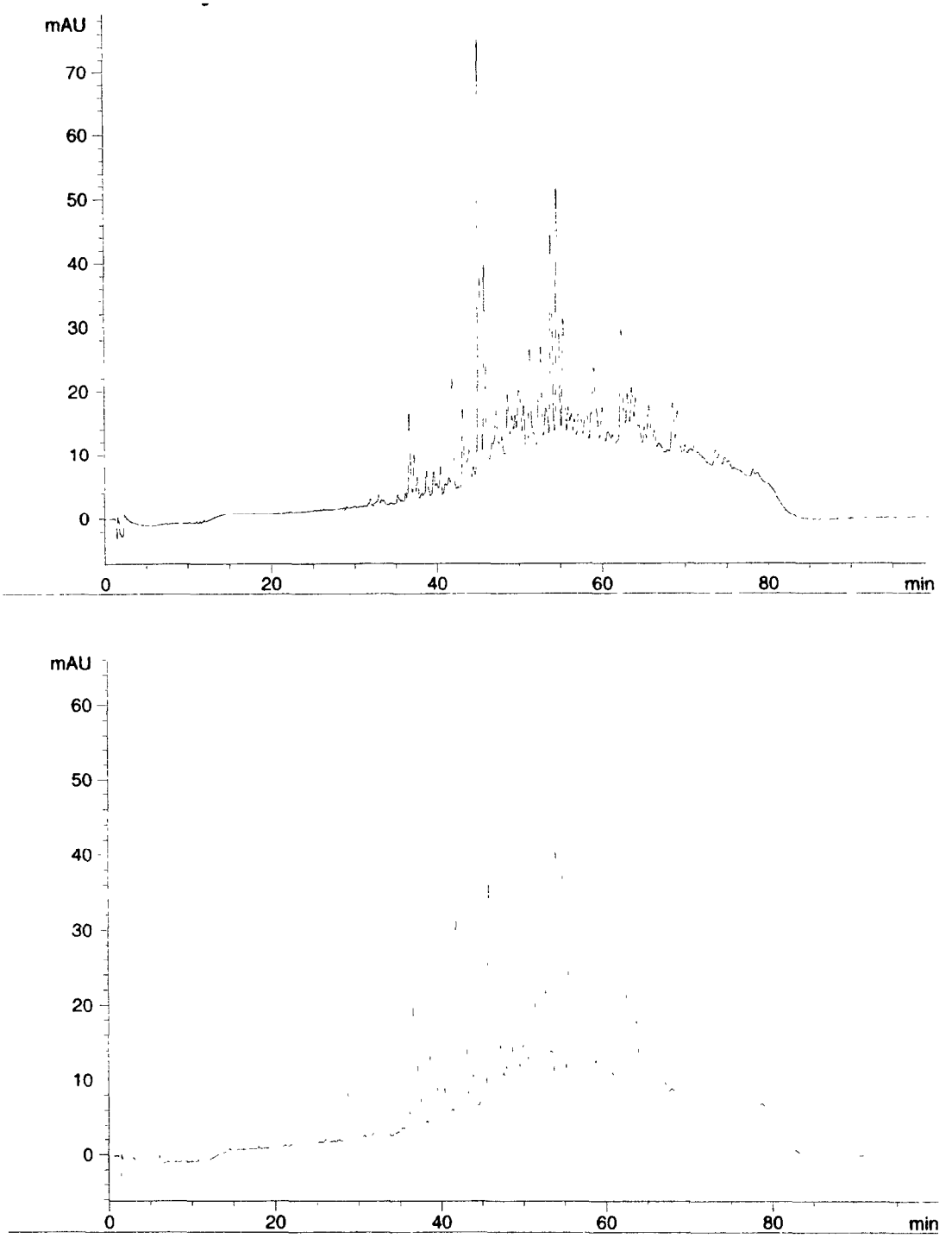

Fig.1 A comparison of chromatogram of entire distribution of oligosaccharides between Amphastar's Enoxaparin (above blue) and Aventis' Lovenox (below red).

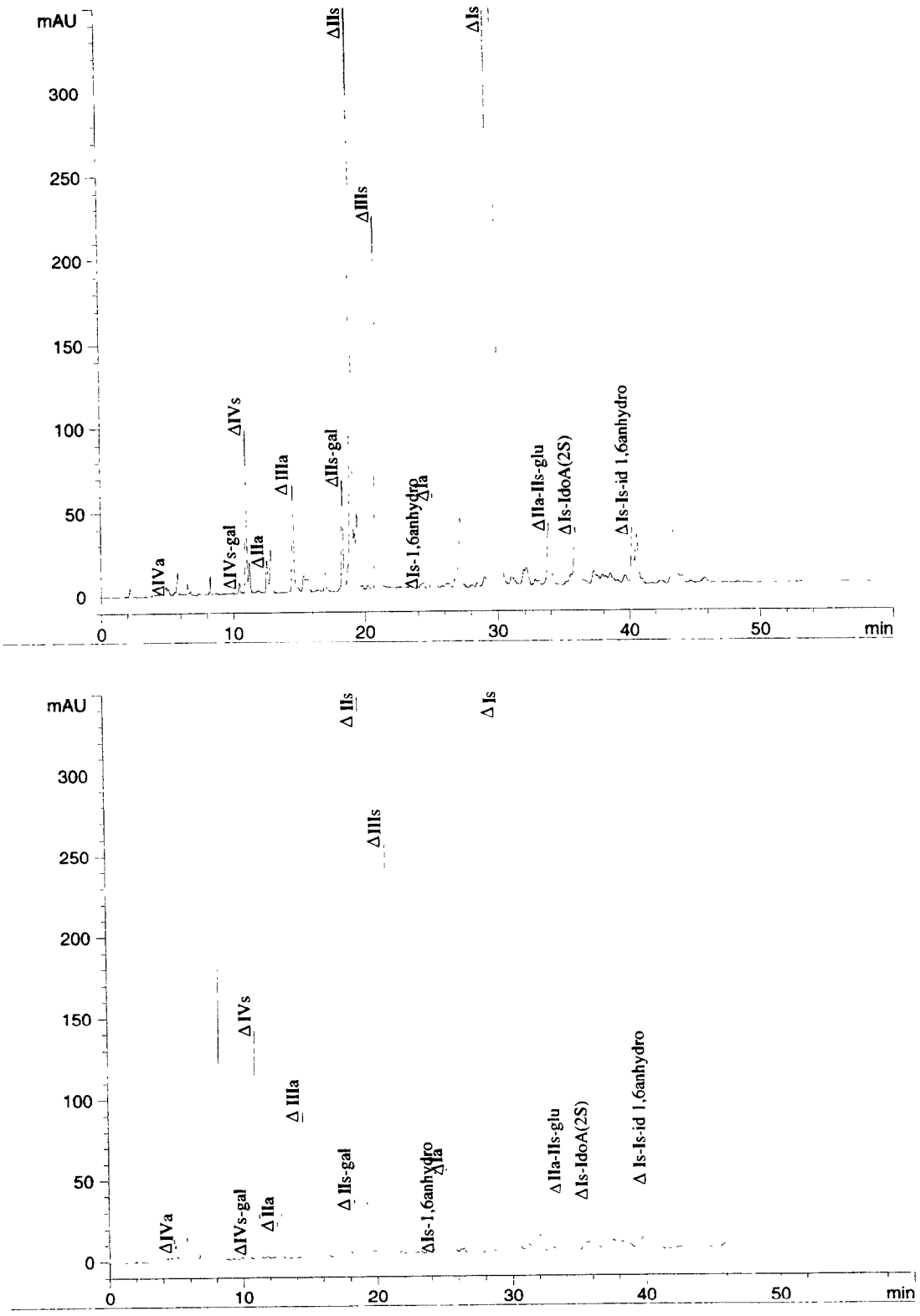

Fig. 2 A comparison of chromatogram of Heparinase-hydrolyzed Enoxaparin between Amphastar's Enoxaparin (above blue) and Aventis' Lovenox (below red).